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Associations of central and peripheral blood pressure with cardiac structure and function in an adolescent birth cohort: the Avon Longitudinal Study of Parents and Children

Diana L. S. Ferreira[1*], MSc, PhD, Abigail Fraser[1, 2*], MA, MPH, PhD, Laura D. Howe [1,2], MSc, PhD, Siana Jones[3], MSc, George Davey Smith[1,2], MA, MD, BChir, MSc, Debbie A. Lawlor[1,2], MBChB, MSc, PhD, Robyn J Tapp[4], Dip, BA, GradDip, PhD, Andy R. Ness[5], BM, BS, MRCP, FFPHM, PhD, John Deanfield[3] BA, BChir, MB, FRCP, Nish Chaturvedi[3], MBBS, MSc, MD, MRCP, Alun D. Hughes[3], MBBS, PhD, FBPharmacolS.

* Authors with equal contributions.

1. School of Social and Community Medicine, University of Bristol, Bristol, UK.
2. MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, UK.
3. Institute of Cardiovascular Sciences, University College London, London, WC1E 6BT, UK
4. Ocular Epidemiology Unit, Department of Optometry and Vision Sciences, The University of Melbourne, Australia
5. National Institute for Health Research (NIHR) Biomedical Research Unit in Nutrition, Diet and Lifestyle at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol and School of Oral and Dental Sciences, University of Bristol

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Reprint requests and corresponding author:

Prof Alun Hughes, Institute of Cardiovascular Sciences, University College London, London, WC1E 6BT, UK

E-mail: alun.hughes@ucl.ac.uk

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Abbreviations:

BP - blood pressure

CVD – cardiovascular disease

MAP - mean arterial pressure

PP - pulse pressure

LVMI - left ventricular mass index

RWT - left ventricular relative wall thickness

LAI - left atrial size indexed to height

BMI - body mass index

SBP – systolic blood pressure

Introduction

The majority of studies relating BP to target organ damage or CVD events have measured BP at a peripheral location, usually the brachial artery. Systolic blood pressure (SBP) and pulse pressure (PP) in the aorta (central BP) are lower than the corresponding peripheral measures[1]. In adults central PP and SBP have been shown to be more closely related to left ventricular mass [2], left ventricular function [3, 4] and CVD events [5] than peripheral pressures.

We compared central and peripheral SBP and their associations with concurrent measures of cardiac structure and function in a large, population based cohort of adolescents (mean age: 17.7 years).

Methods

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective population-based birth cohort study (baseline: 1991-2) (http://www.alspac.bris.ac.uk) [6]. A fully searchable data dictionary is available on http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/. At the age 17 clinic assessment, a random sample (~2,000) of daily clinic attenders underwent echocardiography examinations. Exclusion criteria were pregnancy, congential heart disease or any condition that would prevent participation in the study. Ethical approval was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committee. Participants provided written informed consent.

Sitting peripheral SBP, diastolic BP (DBP), and heart rate were measured in triplicate using standard procedures. Central SBP and DBP were estimated using arterial tonometry (Sphygmocor, Atcor) at the radial artery.

Echocardiography was performed using a HDI 5000 ultrasound machine (Phillips) equipped with a P4-2 Phased Array ultrasound transducer by one of two echocardiographers using a

standard examination protocol. All measurements and calculations were made according to American Society of Echocardiography (ASE) guidelines [7]. On-going quality control was performed throughout the study and reproducibility of echocardiographic measurement was assessed by recalling 30 participants and repeating their measurements. The intra-class correlation of repeated echocardiographic measurements was excellent: 0.75 to 0.93 (intra-observer) and 0.78 to 0.93 (inter-observer).

The following were included as covariates: age at clinic assessment, gender, body mass index (BMI), dual-energy X-ray absorptiometry (DXA) fat mass, accelerometer assessed physical activity at age 15.5, heart rate, and MAP.

Statistical analysis

e′ was positively skewed, and therefore values were logged for analyses. Multivariable linear regression was used to assess associations of central and peripheral SBP with ventricular structure: LVMI, RWT; systolic function: s′, midwall fractional shortening, ejection fraction; and diastolic function: E/e′, mitral E/A ratio, left atrial size index (LAI) and e′ (outcomes). Results were essentially identical when fat mass was replaced with BMI.. We also repeated analyses including in the subgroup for which physical activity data (accelerometer assesses at age 15.5) were available. To compare relationships between central and peripheral BP a bootstrapping procedure (based on 10,000 replications) was used to obtain a P value testing the null hypothesis that the associations of central and peripheral SBP with a given outcome did not differ. There was no strong evidence of exposure-gender interactions; therefore data for males and females were pooled.

Results

Peripheral SBP was higher than its central counterparts (mean difference (SD): 19.7 (4.9)) and the difference increased with increasing SBP. Associations between central and peripheral SBP and measures of cardiac structure and function are presented in the Table. Central and peripheral SBP were positively associated with LVMI, RWT, s′, midwall fractional shortening, LAI, E/A…..

A change in 10 mmHg of central PP was associated with a greater difference in outcome (LVMI, LAI, mitral E/A ratio and e′) than an equivalent change in peripheral PP. Associations remained after adjustment for fat mass (model 2) and further adjustment for MAP and heart rate (model 3). Neither central nor peripheral PP were associated with RWT, midwall fractional shortening, ejection fraction or E/e′.

Results for the subgroup in whom physical activity was assessed were virtually the same as those obtained for the whole study sample (though confidence intervals were wider) and adjusting for physical activity levels did not alter results.

Discussion

Higher PP in peripheral than in central arteries has been attributed to wave reflection from distal peripheral arteries which results in PP amplification. [1, 8] Our observations therefore imply that peripheral wave reflection is more marked in adolescence and extend the findings of a study confined to adults that observed greater amplification of PP with decreasing age [9]. These findings may have important implications for the diagnosis and therapeutic management of hypertension in childhood and adolescence, particularly given that it is now relatively simple to measure central BP with cuff-based devices [10, 11].

Our data demonstrate that central BP is more closely associated with cardiac structure and LV function in adolescence. This may have important implications for the prognostic value of central versus peripheral BP as an indicator of lifetime risk in childhood and adolescence, particularly since low birth weight and rapid increases in adiposity in childhood are associated with higher BP in early adulthood [12]. Previous studies that have examined the relationship between BP and cardiac structure and function in children and adolescents have used peripheral measurements of BP may have underestimated the strength of these associations [13, 14].

In adults, weak associations of peripheral systolic BP and PP with LA size have been reported [15]. We extend these findings to adolescents, showing that even in youth higher PP (particularly central PP) is associated with increased LA size and, by implication, impaired diastolic function and LV filling. Our observation of associations between higher central PP and decreased s' is also suggestive of an early adverse influence of high aortic pulse pressure on systolic function [16], and disturbance of ventricular-arterial coupling [17] even at this young age.

Conclusions

Central PP was markedly lower than peripheral PP in a general adolescent population. Associations with LV structure and function are stronger for central than peripheral pressure. These findings may have important implications for thresholds for the diagnosis and intervention for hypertension in youth, based as it currently is on peripheral measures and re-emphasize the importance of BP as a risk factor in youth.

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Table 1- Multivariate associations of central and peripheral pulse pressure with measurements of ventricular structure, systolic and diastolic function.

Outcomes	Central Pulse Pressure, mmHg		Peripheral Pulse Pressure, mmHg		Bootstrap P-value for the difference between central and peripheral PP
	Mean difference (95% confidence interval) per 10 mmHg	p	Mean difference (95% confidence interval) per 10 mmHg	p	
LEFT VENTRICULAR STRUCTURE					
Left ventricular mass indexed to height$^{2.7}$, g/m$^{2.7}$ (N=1682)					
Model 1	2.17 (1.65, 2.70)	<0.001	1.32 (0.98, 1.66)	<0.001	<0.001
Model 2	1.54 (1.07, 2.02)	<0.001	0.97 (0.66, 1.28)	<0.001	
Model 3	1.00 (0.51, 1.48)	<0.001	0.83 (0.52, 1.13)	<0.001	
Relative wall thickness (N=1682)					
Model 1	0.0002 (-0.005,0.005)	0.96	0.001 (-0.002,0.005)	0.43	0.41
Model 2	-0.0004 (-0.006,0.005)	0.87	0.001 (-0.002,0.004)	0.56	
Model 3	-0.001 (-0.007,0.004)	0.65	0.0005 (-0.003,0.004)	0.77	
SYSTOLIC FUNCTION					
s', cm/s (N=1645)					
Model 1	-0.21 (-0.37, -0.05)	0.01	-0.10 (-0.20, 0.01)	0.07	0.007
Model 2	-0.21 (-0.33, -0.05)	0.01	-0.10 (-0.21, 0.004)	0.06	
Model 3	-0.14 (-0.31, 0.02)	0.09	-0.08 (-0.19, 0.02)	0.12	
Midwall fractional shortening, % (N=1682)					
Model 1	0.06 (-0.13, 0.25)	0.51	0.03 (-0.10, 0.15)	0.68	0.50
Model 2	0.13 (-0.06, 0.32)	0.19	0.07 (-0.06, 0.20)	0.29	
Model 3	0.16 (-0.04, 0.36)	0.11	0.09 (-0.04, 0.21)	0.28	
Ejection Fraction, % (N=1683)					
Model 1	0.16 (-0.40, 0.73)	0.57	0.16 (-0.21, 0.53)	0.44	0.98
Model 2	0.27 (-0.31, 0.84)	0.36	0.23 (-0.14, 0.61)	0.23	
Model 3	0.35 (-0.25, 0.95)	0.25	0.26 (-0.12, 0.64)	0.18	
DIASTOLIC FUNCTION					
Left atrial size indexed to height$^{2.7}$, cm/m$^{2.7}$ (N=1524)					
Model 1	0.03 (0.02, 0.04)	<0.001	0.01 (0.007, 0.02)	<0.001	<0.001
Model 2	0.02 (0.02, 0.03)	<0.001	0.01 (0.008, 0.02)	<0.001	
Model 3	0.02 (0.01, 0.03)	<0.001	0.01 (0.008, 0.02)	<0.001	
Mitral E/A ratio (N=1636)					
Model 1	0.05 (0.02, 0.09)	0.003	0.02 (-0.005, 0.04)	0.06	<0.001
Model 2	0.07 (0.03, 0.10)	<0.001	0.03 (0.009, 0.05)	0.007	
Model 3	0.04 (0.001, 0.07)	0.04	0.03 (0.006, 0.05)	0.01	
Lateral E/e' ratio (N=1625)					
Model 1	0.02 (-0.07, 0.11)	0.66	0.02 (-0.04, 0.08)	0.55	0.82
Model 2	0.05 (-0.04, 0.15)	0.25	0.04 (-0.02, 0.10)	0.19	
Model 3	0.07 (-0.02, 0.17)	0.14	0.04 (-0.02, 0.10)	0.18	

Lateral e', cm/s (N=1645)*					
Model 1	3.13 (1.25, 5.04)	0.001	1.56 (0.35, 2.80)	0.009	0.001
Model 2	3.05 (1.01, 5.13)	0.005	1.32 (0.10, 2.56)	0.03	
Model 3	2.07 (0.12, 4.05)	0.04	1.27 (0.05, 2.50)	0.04	

* Results are percentage difference in outcome per 10 mmHg increase in exposure value.
Model 1: includes age and gender.
Model 2: as in model 1 plus fat mass, height and height squared.
Model 3: as in model 2 plus MAP and heart rate.

Web-table 4. Multivariable associations of central and peripheral systolic blood pressure with measures of ventricular structure, systolic and diastolic function

Outcomes	**Central systolic blood pressure, mmHg**		**Peripheral systolic blood pressure, mmHg**		**Bootstrap P-value**
	Mean difference (95% confidence interval) per 10 mmHg	p	Mean difference (95% confidence interval) per 10 mmHg	p	
LEFT VENTRICULAR STRUCTURE					
Left ventricular mass indexed to height$^{2.7}$, g/m$^{2.7}$ (N=1682)					
Model 1	1.45 (1.13, 1.77)	<0.001	1.35 (1.08, 1.63)	<0.001	0.16
Model 2	0.88 (0.59, 1.18)	<0.001	0.89 (0.64, 1.15)	<0.001	
Model 3	0.93 (0.64, 1.23)	<0.001	0.98 (0.73, 1.23)	<0.001	
Relative wall thickness (N=1694)					
Model 1	0.007 (0.004, 0.01)	<0.001	0.006 (0.003, 0.003)	<0.001	0.20
Model 2	0.007 (0.003, 0.01)	<0.001	0.006 (0.003, 0.009)	<0.001	
Model 3	0.006 (0.003, 0.01)	<0.001	0.006 (0.003, 0.008)	<0.001	
SYSTOLIC FUNCTION					
s', cm/s (N=1657)					
Model 1	-0.08 (-0.18, 0.02)	0.11	-0.06 (-0.15, 0.02)	0.13	0.52
Model 2	-0.09 (-0.19, 0.01)	0.09	-0.07 (-0.16, 0.01)	0.09	
Model 3	-0.09 (-0.19, 0.008)	0.07	-0.09 (-0.17, 0.001)	0.05	
Midwall fractional shortening, % (N=1694)					
Model 1	-0.27 (-0.38, -0.15)	<0.001	-0.20 (-0.30, -0.10)	<0.001	0.01
Model 2	-0.22 (-0.34, -0.10)	<0.001	-0.16 (-0.26, -0.06)	0.003	
Model 3	-0.22 (-0.34, -0.10)	<0.001	-0.15 (-0.25, -0.05)	0.005	
Ejection Fraction, % (N=1695)					
Model 1	-0.32 (-0.67, 0.02)	0.07	-0.20 (-0.49, 0.10)	0.20	0.10
Model 2	-0.24 (-0.60, 0.12)	0.19	-0.11 (-0.42, 0.20)	0.48	
Model 3	-0.24 (-0.60, 0.12)	0.19	-0.11 (-0.42, 0.20)	0.50	
DIASTOLIC FUNCTION					
Left atrial size indexed to height$^{2.7}$, cm/m$^{2.7}$ (N=1524)					
Model 1	0.007 (0.0003, 0.01)	0.04	0.007 (0.001, 0.01)	0.02	0.95
Model 2	0.004 (-0.001, 0.009)	0.11	0.006 (0.001, 0.01)	0.01	
Model 3	0.005 (-0.008, 0.001)	0.05	0.007 (0.003, 0.01)	0.001	
Mitral E/A ratio (N=1648)					
Model 1	-0.04 (-0.07, -0.02)	<0.001	-0.03 (-0.05, -0.01)	0.001	0.003
Model 2	-0.03 (-0.05, -0.01)	0.004	-0.02 (-0.04, -0.001)	0.04	
Model 3	-0.03 (-0.05, -0.01)	0.009	-0.01 (-0.03, 0.01)	0.22	

Lateral E/e' ratio (N=1637)					
Model 1	0.007 (-0.06, 0.06)	0.96	0.003 (-0.04, 0.05)	0.91	0.79
Model 2	0.03 (-0.02, 0.09)	0.25	0.03 (-0.02, 0.08)	0.18	
Model 3	0.03 (-0.03, 0.09)	0.27	0.03 (-0.02, 0.08)	0.22	
Lateral e', cm/s (N=1657)*					
Model 1	-0.05 (-1.17, 1.10)	0.91	0.19 (-0.80, 1.17)	0.70	0.34
Model 2	-0.60 (-1.79, 0.54)	0.29	-0.27 (-1.27, 0.74)	0.61	
Model 3	-0.53 (-1.67, 0.64)	0.37	-0.06 (-1.06, 0.94)	0.90	

* Results are percent difference in outcome per 10 mmHg increase in exposure value.
Model 1: includes age and gender.
Model 2: as in model 1 plus fat mass, height and height squared.
Model 3: as in model 2 plus heart rate.